

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 HL 00012-05 LBG												
PERIOD COVERED October 1, 1978 - September 30, 1979														
TITLE OF PROJECT (30 characters or less) Muscarinic Acetylcholine Receptors of Cultured Cell Lines														
NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT <table border="0" data-bbox="87 485 1143 604"> <tr> <td>PI:</td> <td>Marshall Nirenberg</td> <td>Chief, LBG</td> <td>LBG NHLBI</td> </tr> <tr> <td>OTHER:</td> <td>William L. Kline</td> <td>Guest Worker</td> <td>LBG NHLBI</td> </tr> <tr> <td></td> <td>Orest Hurko</td> <td>Staff Associate</td> <td>LBG NHLBI</td> </tr> </table>			PI:	Marshall Nirenberg	Chief, LBG	LBG NHLBI	OTHER:	William L. Kline	Guest Worker	LBG NHLBI		Orest Hurko	Staff Associate	LBG NHLBI
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OTHER:	William L. Kline	Guest Worker	LBG NHLBI											
	Orest Hurko	Staff Associate	LBG NHLBI											
COOPERATING UNITS (if any) None														
LAB/BRANCH Laboratory of Biochemical Genetics														
SECTION Section on Molecular Biology														
INSTITUTE AND LOCATION NHLBI, NIH, Bethesda, MD 20205														
TOTAL MANYEARS: 0.25	PROFESSIONAL: 0.25	OTHER: 0												
CHECK APPROPRIATE BOX(ES) <input type="checkbox"/> (a) HUMAN SUBJECTS <input type="checkbox"/> (b) HUMAN TISSUES <input checked="" type="checkbox"/> (c) NEITHER <input type="checkbox"/> (a1) MINORS <input type="checkbox"/> (a2) INTERVIEWS														
SUMMARY OF WORK (200 words or less - underline keywords) Studies on <u>muscarinic acetylcholine receptors</u> focus both on ligand-binding and on defining the physical properties of muscarinic receptors.														

1076

Project Description:

Major Findings: [³H]-Quinuclidinyl-benzilate (QNB) was used to study muscarinic acetylcholine receptors in NG108-15 membrane preparations. The apparent dissociation constant of [³H]QNB is 1×10^{-10} M; the average NG108-15 cell possesses 30,000 specific sites for [³H]-QNB. Activation of the receptors with acetylcholine or carbachol results in cell depolarization, a small increase in cellular cGMP, and inhibition of adenylate cyclase. Cell depolarization and rise in cGMP levels desensitize in 30 sec; whereas, the inhibition of adenylate cyclase does not desensitize. Scatchard analysis revealed only one homogeneous class of [³H]-QNB binding sites; however biphasic rates of [³H]-QNB association with and dissociation from receptors were found. Evidence was obtained for the formation of a dissociable [[³H]-QNB·Receptor] complex which then is converted to a form which dissociates only slowly. Hill coefficients of approximately 1.0 were found for receptor antagonists and approximately 0.5 for receptor activators. A sequential series of reactions were proposed to account for these observations and for the various states of the muscarinic acetylcholine receptor that were detected.

Publications:

1. Burgermeister, W., Kline, W.L., Nirenberg, M., and Witkop, B., Mol. Pharm. 14, 751-767 (1978).
2. Hurko, O. Specific [³H]-Quinuclidinyl Benzilate binding activity in digitonin-solubilized preparations for bovine brain. Arch. Biochem. and Biophys. 190, 434-445 (1978).